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=> S (Common gamma chain)

L1 3627 (COMMON GAMMA CHAIN)

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=> S (variant or mutant or mutated or mutation or mutating or mutagenesis or
substitution or substitute or substituted or substituting or replace or replaced or
replacing or replacement or exchange or exchanged)
L2 10181735 (VARIANT OR MUTANT OR MUTATED OR MUTATION OR MUTATING OR MUTAGEN
ESIS OR SUBSTITUTION OR SUBSTITUTE OR SUBSTITUTED OR SUBSTITUTIN
G OR REPLACE OR REPLACED OR REPLACING OR REPLACEMENT OR EXCHANGE
OR EXCHANGED)

=> s l1 (100A) l2
L3 271 L1 (100A) L2

=> s l2 (6A) (Activity or action or effect or function)
L4 554458 L2 (6A) (ACTIVITY OR ACTION OR EFFECT OR FUNCTION)

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L5 13 L3 AND L4

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BIOTECHNO, WPIDS, DISSABS'
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=> s l7 or l8
L9 8 L7 OR L8

=> d l9 1-8 bib ab

L9 ANSWER 1 OF 8 LIFESCI COPYRIGHT 2010 CSA on STN
AN 2008:270375 LIFESCI
TI The Crystal Structure of CHIR-AB1: A Primordial Avian Classical Fc
Receptor
AU Arnon, T.I.; Kaiser, J.T.; West, A.P.; Olson, R.; Diskin, R.; Viertlboeck,
B.C.; Gobel, T.W.; Bjorkman, P.J.
CS 114-96 and Howard Hughes Medical Institute, California Institute of
Technology, Pasadena, CA 91125, USA; E-mail: bjorkman@caltech.edu
SO Journal of Molecular Biology [J. Mol. Biol.], (20080912) vol. 381, no. 4,
pp. 1012-1024.
ISSN: 0022-2836.
DT Journal
FS F
LA English
SL English
AB CHIR-AB1 is a newly identified avian immunoglobulin (Ig) receptor that
includes both activating and inhibitory motifs and was therefore
classified as a potentially bifunctional receptor. Recently, CHIR-AB1 was

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shown to bind the Fc region of chicken IgY and to induce calcium mobilization via association with the common gamma - chain, a subunit that transmits signals upon ligation of many different immunoreceptors. Here we describe the 1.8-A-resolution crystal structure of the CHIR-AB1 ectodomain. The receptor ectodomain consists of a single C2-type Ig domain resembling the Ig-like domains found in mammalian Fc receptors such as Fc gamma Rs and Fc alpha RI. Unlike these receptors and other monomeric Ig superfamily members, CHIR-AB1 crystallized as a 2-fold symmetrical homodimer that bears no resemblance to variable or constant region dimers in an antibody. Analytical ultracentrifugation demonstrated that CHIR-AB1 exists as a mixture of monomers and dimers in solution, and equilibrium gel filtration revealed a 2:1 receptor/ligand binding stoichiometry. Measurement of the 1:1 CHIR-AB1/IgY interaction affinity indicates a relatively low affinity complex, but a 2:1 CHIR-AB1/IgY interaction allows an increase in apparent affinity due to avidity effects when the receptor is tethered to a surface. Taken together, these results add to the structural understanding of Fc receptors and their functional mechanisms.

L9 ANSWER 2 OF 8 LIFESCI COPYRIGHT 2010 CSA on STN
 AN 2005:64525 LIFESCI
 TI The Structure of Interleukin-2 Complexed with Its Alpha Receptor
 AU Rickert, Mathias; Wang, Xinquan; Boulanger, Martin J.; Goriatheva, Natalia; Garcia, K. Christopher
 CS Departments of Microbiology and Immunology, and Structural Biology, Stanford University School of Medicine, 299 Campus Drive, Fairchild D319, Stanford, CA 94305-5124, USA.; E-mail: kcgarcia@stanford.edu
 SO Science (Washington) [Science (Wash.)], (20050603) vol. 308, no. 5727, pp. 1477-1480.
 ISSN: 0036-8075.
 DT Journal
 FS F
 LA English
 SL English
 AB Interleukin-2 (IL-2) is an immunoregulatory cytokine that binds sequentially to the alpha (IL-2R alpha), beta (IL-2R beta), and common gamma chain (gamma sub(c)) receptor subunits. Here we present the 2.8 angstrom crystal structure of a complex between human IL-2 and IL-2R alpha , which interact in a docking mode distinct from that of other cytokine receptor complexes. IL- 2R alpha is composed of strand-swapped "sushi-like" domains, unlike the classical cytokine receptor fold. As a result of this domain swap, IL-2R alpha uses a composite surface to dock into a groove on IL-2 that also serves as a binding site for antagonist drugs. With this complex, we now have representative structures for each class of hematopoietic cytokine receptor-docking modules.

L9 ANSWER 3 OF 8 LIFESCI COPYRIGHT 2010 CSA on STN
 AN 1999:65416 LIFESCI
 TI Crystal Structure of the Interleukin-4/Receptor alpha Chain Complex Reveals a Mosaic Binding Interface
 AU Hage, T.; Sebald, W.; Reinemer, P.
 CS Institut fuer Physiologische Chemie II, Theodor-Boveri-Institut fuer Biowissenschaften (Biozentrum), Universitaet Wuerzburg, Am Hubland, D-97074 Wuerzburg, Germany; E-mail: sebald@biozentrum.uni-wuerzburg.de
 SO Cell, (19990415) vol. 97, no. 2, pp. 271-281.
 ISSN: 0092-8674.
 DT Journal
 FS F
 LA English
 SL English

AB Interleukin-4 (IL-4) is a principal regulatory cytokine during an immune response and a crucial determinant for allergy and asthma. IL-4 binds with high affinity and specificity to the ectodomain of the IL-4 receptor alpha chain (IL4-BP). Subsequently, this intermediate complex recruits the common gamma chain (gamma c), thereby initiating transmembrane signaling. The crystal structure of the intermediate complex between human IL-4 and IL4-BP was determined at 2.3 Å resolution. It reveals a novel spatial orientation of the two proteins, a small but unexpected conformational change in the receptor-bound IL-4, and an interface with three separate clusters of trans-interacting residues. Novel insights on ligand binding in the cytokine receptor family and a paradigm for receptors of IL-2, IL-7, IL-9, and IL-15, which all utilize gamma c, are provided.

L9 ANSWER 4 OF 8 Elsevier Biobase COPYRIGHT 2010 Elsevier Science B.V. on STN

AN 2008208091 ESBIOBASE

TI The Crystal Structure of CHIR-AB1: A Primordial Avian Classical Fc Receptor

AU Arnon, Tal I.; Kaiser, Jens T.; West Jr., Anthony P.; Olson, Rich; Diskin, Ron; Bjorkman, Pamela J.; Viertlboeck, Birgit C.; Gobel, Thomas W.

CS Arnon, Tal I.; Kaiser, Jens T.; West Jr., Anthony P.; Olson, Rich; Diskin, Ron; Bjorkman, Pamela J. (Division of Biology, 114-96 and Howard Hughes Medical Institute, California Institute of Technology, Pasadena, CA 91125 (US)); Viertlboeck, Birgit C.; Gobel, Thomas W. (Institute of Animal Physiology, University of Munich, Munich, 80539 (DE))
EMAIL: bjorkman@caltech.edu

SO Journal of Molecular Biology (12 Sep 2008) Volume 381, Number 4, pp. 1012-1024, 58 refs.
CODEN: JMOBAK ISSN: 0022-2836
DOI: 10.1016/j.jmb.2008.06.082
Published by: Academic Press, 24-28 Oval Road, London, NW1 7DX (GB)

PUI S0022283608008097

CY United Kingdom

DT Journal; Article

LA English

SL English

ED Entered STN: 18 Feb 2009
Last updated on STN: 18 Feb 2009

AB CHIR-AB1 is a newly identified avian immunoglobulin (Ig) receptor that includes both activating and inhibitory motifs and was therefore classified as a potentially bifunctional receptor. Recently, CHIR-AB1 was shown to bind the Fc region of chicken IgY and to induce calcium mobilization via association with the common gamma chain, a subunit that transmits signals upon ligation of many different immunoreceptors. Here we describe the 1.8-Å-resolution crystal structure of the CHIR-AB1 ectodomain. The receptor ectodomain consists of a single C2-type Ig domain resembling the Ig-like domains found in mammalian Fc receptors such as FcγRs and FcαRI. Unlike these receptors and other monomeric Ig superfamily members, CHIR-AB1 crystallized as a 2-fold symmetrical homodimer that bears no resemblance to variable or constant region dimers in an antibody. Analytical ultracentrifugation demonstrated that CHIR-AB1 exists as a mixture of monomers and dimers in solution, and equilibrium gel filtration revealed a 2:1 receptor/ligand binding stoichiometry. Measurement of the 1:1 CHIR-AB1/IgY interaction affinity indicates a relatively low affinity complex, but a 2:1 CHIR-AB1/IgY interaction allows an increase in apparent affinity due to avidity effects when the receptor is tethered to a surface. Taken together, these results add to the structural understanding of Fc receptors and

their functional mechanisms. .COPYRG. 2008 Elsevier Ltd. All rights reserved.

- L9 ANSWER 5 OF 8 Elsevier Biobase COPYRIGHT 2010 Elsevier Science B.V. on STN
- AN 2005202146 ESIIOBASE
- TI Crystal structure of the Jak3 kinase domain in complex with a staurosporine analog
- AU Eck, Michael J.; Boggon, Titus J.; Li, Yiqun; Manley, Paul W.
- CS Eck, Michael J. (Dana-Farber Cancer Institute, 44 Binney St, Boston, MA 02115 (US)); Boggon, Titus J.; Li, Yiqun; Manley, Paul W.
EMAIL: eck@red.dfci.harvard.edu
- SO Blood (1 Aug 2005) Volume 106, Number 3, pp. 996-1002, 39 refs.
CODEN: BLOOAW ISSN: 0006-4971
DOI: 10.1182/blood-2005-02-0707
- CY United States of America
- DT Journal; Article
- LA English
- SL English
- ED Entered STN: 3 Feb 2009
Last updated on STN: 3 Feb 2009
- AB Jak (Janus kinase) family nonreceptor tyrosine kinases are central mediators of cytokine signaling. The Jak kinases exhibit distinct cytokine receptor association profiles and so transduce different signals. Jak3 expression is limited to the immune system, where it plays a key role in signal transduction from cytokine receptors containing the common gamma-chain, γ_c . Patients unable to signal via γ_c present with severe combined immunodeficiency (SCID). The finding that Jak3 mutations result in SCID has made it a target for development of lymphocyte-specific immunosuppressants. Here, we present the crystal structure of the Jak3 kinase domain in complex with staurosporine analog AFN941. The kinase domain is in the active conformation, with both activation loop tyrosine residues phosphorylated. The phosphate group on pTyr981 in the activation loop is in part coordinated by an arginine residue in the regulatory C-helix, suggesting a direct mechanism by which the active position of the C-helix is induced by phosphorylation of the activation loop. Such a direct coupling has not been previously observed in tyrosine kinases and may be unique to Jak kinases. The crystal structure provides a detailed view of the Jak3 active site and will facilitate computational and structure-directed approaches to development of Jak3-specific inhibitors. .COPYRG. 2005 by The American Society of Hematology.
- L9 ANSWER 6 OF 8 Elsevier Biobase COPYRIGHT 2010 Elsevier Science B.V. on STN
- AN 2005150714 ESIIOBASE
- TI Structural Biology: The structure of interleukin-2 complexed with its alpha receptor
- AU Rickert, Mathias; Wang, Xinquan; Boulanger, Martin J.; Goriatcheva, Natalia; Garcia, K. Christopher
- CS Rickert, Mathias; Wang, Xinquan; Boulanger, Martin J.; Goriatcheva, Natalia; Garcia, K. Christopher (Department of Microbiology and Immunology, Stanford University School of Medicine, Fairchild D319, 299 Campus Drive, Stanford, CA 94305-5124 (US))
EMAIL: kcgarcia@stanford.edu
- SO Science (3 Jun 2005) Volume 308, Number 5727, pp. 1477-1480, 33 refs.
CODEN: SCIEAS ISSN: 0036-8075
DOI: 10.1126/science.1109745
- CY United States of America
- DT Journal; Article

LA English
 SL English
 ED Entered STN: 3 Feb 2009
 Last updated on STN: 3 Feb 2009

AB Interleukin-2 (IL-2) is an immunoregulatory cytokine that binds sequentially to the alpha (IL-2R α), beta (IL-2R β), and common gamma chain (γ c) receptor subunits. Here we present the 2.8 angstrom crystal structure of a complex between human IL-2 and IL-2R α , which interact in a docking mode distinct from that of other cytokine receptor complexes. IL-2R α is composed of strand-swapped "sushi-like" domains, unlike the classical cytokine receptor fold. As a result of this domain swap, IL-2R α uses a composite surface to dock into a groove on IL-2 that also serves as a binding site for antagonist drugs. With this complex, we now have representative structures for each class of hematopoietic cytokine receptor-docking modules.

L9 ANSWER 7 OF 8 Elsevier Biobase COPYRIGHT 2010 Elsevier Science B.V. on STN
 AN 1999096764 ESBIODBASE
 TI Crystal structure of the interleukin-4/receptor α chain complex reveals a mosaic binding interface
 AU Hage, Thorsten; Sebald, Walter; Reinemer, Peter
 CS Hage, Thorsten; Sebald, Walter (Institut fur Physiologische Chemie II, Theodor-Boveri-Institut fur Biowissenschaften (Biozentrum), Universitat Wurzburg, Am Hubland, D-97074 Wurzburg (DE)); Reinemer, Peter (Bayer AG, Pharmaforschung (PH-R LSC-NP), Postfach 101709, D-42096 Wuppertal (DE))
 EMAIL: sebald@biozentrum.uni-wuerzburg.de
 SO Cell (16 Apr 1999) Volume 97, Number 2, pp. 271-281, 57 refs.
 CODEN: CELLB5 ISSN: 0092-8674
 CY United States of America
 DT Journal; Article
 LA English
 SL English
 ED Entered STN: 31 Jan 2009
 Last updated on STN: 31 Jan 2009

AB Interleukin-4 (IL-4) is a principal regulatory cytokine during an immune response and a crucial determinant for allergy and asthma. IL-4 binds with high affinity and specificity to the ectodomain of the IL-4 receptor α chain (IL4-BP). Subsequently, this intermediate complex recruits the common γ chain (γ c), thereby initiating transmembrane signaling. The crystal structure of the intermediate complex between human IL-4 and IL4-BP was determined at 2.3 Å resolution. It reveals a novel spatial orientation of the two proteins, a small but unexpected conformational change in the receptor-bound IL-4, and an interface with three separate clusters of trans-interacting residues. Novel insights on ligand binding in the cytokine receptor family and a paradigm for receptors of IL-2, IL-7, IL-9, and IL-15, which all utilize γ c, are provided.

L9 ANSWER 8 OF 8 BIOTECHNO COPYRIGHT 2010 Elsevier Science B.V. on STN
 AN 1999:29194277 BIOTECHNO
 TI Crystal structure of the interleukin-4/receptor α chain complex reveals a mosaic binding interface
 AU Hage T.; Sebald W.; Reinemer P.
 CS W. Sebald, Inst. fur Physiologische Chemie II, T.-Boveri-Inst. Biowissenschaften, Universitat Wurzburg, Am Hubland, D-97074 Wurzburg, Germany.
 E-mail: sebald@biozentrum.uni-wuerzburg.de
 SO Cell, (16 APR 1999), 97/2 (271-281), 54 reference(s)

CODEN: CELLB5 ISSN: 0092-8674

DT Journal; Article

CY United States

LA English

SL English

AB Interleukin-4 (IL-4) is a principal regulatory cytokine during an immune response and a crucial determinant for allergy and asthma. IL-4 binds with high affinity and specificity to the ectodomain of the IL-4 receptor α chain (IL4-BP). Subsequently, this intermediate complex recruits the common γ chain (γ c), thereby initiating transmembrane signaling. The crystal structure of the intermediate complex between human IL-4 and IL4-BP was determined at 2.3 Å resolution. It reveals a novel spatial orientation of the two proteins, a small but unexpected conformational change in the receptor-bound IL-4, and an interface with three separate clusters of trans- interacting residues. Novel insights on ligand binding in the cytokine receptor family and a paradigm for receptors of IL-2, IL-7, IL-9, and IL-15, which all utilize γ c, are provided.

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L6 ANSWER 1 OF 6 DISSABS COPYRIGHT (C) 2010 ProQuest Information and Learning Company; All Rights Reserved on STN

AN 2009:39707 DISSABS Order Number: AAI3341807

TI IL-7R and c-Kit signaling in thymopoiesis

AU Toyama, Akira [Ph.D.]; Lutzko, Carolyn [advisor]

CS University of Southern California (0208)

SO Dissertation Abstracts International, (2008) Vol. 70, No. 1B, p. 48. Order No.: AAI3341807. 77 pages.

ISBN: 978-0-549-97577-9.

DT Dissertation

FS DAI

LA English

ED Entered STN: 20090730

Last Updated on STN: 20090730

AB < Pub Inc> IL-7 and Kit ligand (KL) are cytokines produced by thymic epithelial cells, which interact with their cognate receptors on immature thymocytes. The IL-7R is comprised of the IL-7Ra and common γ chain (γ c) and has no intrinsic kinase activity, while KL binds to the receptor tyrosine kinase Kit. Both IL-7Ra $^{-/-}$ and IL-7 $^{-/-}$ mice have profound defects in thymopoiesis, although for unexplained reasons, the defects in differentiation and thymic cellularity are more severe for IL-7Ra $^{-/-}$ than IL-7 $^{-/-}$ mice. In order to understand possible interactions between IL-7R and Kit signaling in vivo, we generated doubly mutated mice which were homozygous for the Kit W41 loss of function mutation and null for either IL-7 or IL-7Ra. While IL-7 $^{-/-}$ and IL-7Ra $^{-/-}$ mice had a 90-99% reduction in thymic cellularity and the KitW41/W41 mice had a 50% reduction, the IL-7 $^{-/-}$ KitW41/W41 and IL-7Ra $^{-/-}$ KitW41/W41 mice had fewer than 200 thymocytes, representing a 5-6 log decrease in thymic cellularity. The thymocytes in the IL-7 $^{-/-}$ KitW41/W41 and IL-7Ra $^{-/-}$ KitW41/W41 mice were blocked at the earliest recognizable stage of thymic differentiation. The frequency of early T-lineage progenitors (ETP) in IL-7Ra $^{-/-}$, IL-7 $^{-/-}$ KitW41/W41, and IL-7Ra $^{-/-}$ KitW41/W41 mice was significantly reduced compared to parental strains or wild type mice. Introduction of a bcl-2 transgene did not relieve the block in differentiation of CD4-CD8 $^{-}$ (DN) thymocytes, or

reduction in ETP absolute numbers in IL-7Ra^{-/-}Kit W41/W41 mice, but partially rescued IL-7Ra^{-/-} mice. Cytokeratin expression analysis showed that thymic epithelial cells (TEC) of IL-7^{-/-}Kit W41/W41, and IL-7Ra^{-/-}Kit W41/W41 mice were K8+K5⁺, indicating that differentiation of TEC was arrested in these mice. IL-7Ra^{-/-}Kit W41/W41 transgenic bcl-2 thymuses had K8+K5⁻ areas indicating that medullary areas developed. Conclusions: (1) IL-7R and Kit provide synergistic, partially redundant, and unique signals for thymocyte proliferation, maintenance, and differentiation; (2) the less severe defect in IL-7^{-/-} mice is due to partial complementation by Kit, possibly by direct interaction between IL-7R and Kit; (3) a functional Kit pathway is required in order for the bcl-2 transgene to partially rescue IL-7Ra^{-/-} mice; (4) although ETP do not express IL-7R, they are dependent on IL-7R signaling for generation.

L6 ANSWER 2 OF 6 WPIDS COPYRIGHT 2010 THOMSON REUTERS on STN
AN 2003-845333 [200378] WPIDS
CR 2003-845330
DNC C2003-237596 [200378]
TI New nuclear factor inducing kinase or its mutein, variant, fusion protein, functional derivative, circularly permuted derivative or fragment, useful for treating an autoimmune disease, infarct, Alzheimer's disease or atherosclerosis
DC B04; D16
IN RAMAKRISHNAN P; SHMUSHKOVICH T; WALLACH D; SCHMUSHKOVICH T
PA (YEDA-C) YEDA RES & DEV CO LTD; (YEDA-C) YEDA RES&DEV CO LTD
CYC 102
PIA WO 2003087380 A1 20031023 (200378)* EN 98[16]
AU 2003226607 A1 20031027 (200436) EN
EP 1499729 A1 20050126 (200508) EN
JP 2005530491 W 20051013 (200568) JA 57
US 20050272633 A1 20051208 (200580) EN
AU 2003226607 B2 20090205 (200952) EN
JP 4435575 B2 20100317 (201020) JA 47
ADT WO 2003087380 A1 WO 2003-IL317 20030415; AU 2003226607 A1 AU 2003-226607 20030415; AU 2003226607 B2 AU 2003-226607 20030415; EP 1499729 A1 EP 2003-746399 20030415; JP 2005530491 W JP 2003-584319 20030415; EP 1499729 A1 WO 2003-IL317 20030415; JP 2005530491 W WO 2003-IL317 20030415; US 20050272633 A1 WO 2003-IL317 20030415; US 20050272633 A1 US 2005-511314 20050517; JP 4435575 B2 JP 2003-584319 20030415; JP 4435575 B2 PCT Application WO 2003-IL317 20030415
FDT AU 2003226607 A1 Based on WO 2003087380 A; EP 1499729 A1 Based on WO 2003087380 A; JP 2005530491 W Based on WO 2003087380 A; AU 2003226607 B2 Based on WO 2003087380 A; JP 4435575 B2 Previous Publ JP 2005530491 W; JP 4435575 B2 Based on WO 2003087380 A
PRAI IL 2002-152183 20021008
IL 2002-149217 20020418
AB WO 2003087380 A1 UPAB: 20060203
NOVELTY - A NIK (nuclear factor (NF)-kB-inducing kinase) or its mutein, variant, fusion protein, functional derivative, circularly permuted derivative or fragment, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:
(1) a DNA encoding NIK or its mutein, variant, fusion protein, functional derivative, circularly permuted derivative or fragment;
(2) an antibody specific to the NIK or its mutein, variant, fusion protein, functional derivative, circularly permuted derivative or fragment;
(3) a small molecule capable of modulating the interaction between interleukin 2 (IL-2) common gamma chain (cgammac) and NIK kinase (NIKK), where the small molecule is obtainable by screening products of combinatorial chemistry in a luciferase system;

(4) treating a disease involving signaling of a cytokine through IL-2 cgammac in the pathogenesis of the disease comprising administering the NIK or its mutein, variant, fusion protein, functional derivative, circularly permuted derivative or fragment, DNA, small molecule or antibody;

(5) a pharmaceutical composition comprising the NIK or its mutein, variant, fusion protein, functional derivative, circularly permuted derivative or fragment, DNA, small molecule and antibody;

(6) a polypeptide fragment of NIK, comprising the IL-2R cgammac binding domain, or its mutein, variant, fusion protein, functional derivative, circularly permuted derivative or its fragment;

(7) a DNA encoding the polypeptide fragment of NIK;

(8) a vector comprising the DNA;

(9) a cell comprising the vector;

(10) producing NIK polypeptide comprising culturing the cell, and collecting the polypeptide produced; and

(11) an antibody, polyclonal or monoclonal, its chimeric antibody, fully humanized antibody, anti-anti-Id antibody, intrabody or its fragment that specifically recognizes and binds the polypeptide fragment of NIK.

ACTIVITY - Antiinflammatory; Gastrointestinal-Gen; Antiarthritic; Antirheumatic; Osteopathic; Antiasthmatic; Cardiant; Nootropic; Neuroprotective; Antiarteriosclerotic; Immunosuppressive; Antianemic; Antithyroid. No biological data given.

MECHANISM OF ACTION - Gene Therapy. No biological data given.

USE - The NIK or its mutein, variant, fusion protein, functional derivative, circularly permuted derivative or fragment, DNA, small molecule and antibody are useful for modulating the interaction between interleukin 2 (IL-2) common gamma chain (cgammac) and NIK; and for the manufacture of a medicament for the treatment of a disease, e.g. a disease resulting from excessive immune response such as rheumatoid arthritis, osteoarthritis, inflammatory bowel disease, asthma, cardiac infarct, Alzheimer's disease or atherosclerosis; or an autoimmune disease such as immune thyroiditis, or other arthropaties, such as autoimmune hemolytic anemia. The small molecule is useful for modulating signaling through cgammac (all claimed).

L6 ANSWER 3 OF 6 WPIDS COPYRIGHT 2010 THOMSON REUTERS on STN
AN 2003-845330 [200378] WPIDS
CR 2003-845333
DNC C2003-237593 [200378]
TI New interleukin-2 common gamma chain or its
mutein, variant, fusion protein, functional derivative,
circularly permuted derivative or fragment useful for treating
Alzheimer's disease or atherosclerosis
DC B04; D16
IN RAMAKRISHNAN P; SHMUSHKOVICH T; WALLACH D
PA (YEDA-C) YEDA RES & DEV CO LTD; (YEDA-C) YEDA RES&DEV CO LTD
CYC 102
PIA WO 2003087374 A1 20031023 (200378)* EN 103[16]
AU 2003222415 A1 20031027 (200436) EN
EP 1499724 A1 20050126 (200508) EN
JP 2005525113 W 20050825 (200560) JA 59
US 20050287144 A1 20051229 (200603) EN
US 7416730 B2 20080826 (200857) EN
US 20090042796 A1 20090212 (200919) EN
AU 2003222415 B2 20090205 (200952) EN
JP 4435574 B2 20100317 (201020) JA 47
ADT WO 2003087374 A1 WO 2003-IL316 20030415; AU 2003222415 A1 AU 2003-222415
20030415; AU 2003222415 B2 AU 2003-222415 20030415; EP 1499724 A1 EP
2003-717504 20030415; JP 2005525113 W JP 2003-584315 20030415; EP 1499724
A1 WO 2003-IL316 20030415; JP 2005525113 W WO 2003-IL316 20030415; US

20050287144 A1 WO 2003-IL316 20030415; US 7416730 B2 WO 2003-IL316 20030415; US 20090042796 A1 Div Ex WO 2003-IL316 20030415; US 20050287144 A1 US 2005-511722 20050622; US 7416730 B2 US 2005-511722 20050622; US 20090042796 A1 Div Ex US 2005-511722 20050622; US 20090042796 A1 US 2008-166110 20080701; JP 4435574 B2 JP 2003-584315 20030415; JP 4435574 B2 PCT Application WO 2003-IL316 20030415

FDT US 20090042796 A1 Div Ex US 7416730 B; AU 2003222415 A1 Based on WO 2003087374 A; EP 1499724 A1 Based on WO 2003087374 A; JP 2005525113 W Based on WO 2003087374 A; US 7416730 B2 Based on WO 2003087374 A; AU 2003222415 B2 Based on WO 2003087374 A; JP 4435574 B2 Previous Publ JP 2005525113 W; JP 4435574 B2 Based on WO 2003087374 A

PRAI IL 2002-152183 20021008
IL 2002-149217 20020418

AB WO 2003087374 A1 UPAB: 20060120
NOVELTY - An interleukin 2 (IL-2) common gamma chain (cgammac) or its mutein, variant, fusion protein, functional derivative, circularly permuted derivative or fragment, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

- (1) a DNA encoding cgammac or its mutein, variant, fusion protein, functional derivative, circularly permuted derivative or fragment;
 - (2) an antibody specific to the cgammac or its mutein, variant, fusion protein, functional derivative, circularly permuted derivative or fragment;
 - (3) a small molecule capable of modulating the interaction between IL-2 common gamma chain (cgammac) and nuclear factor kB inducing kinase (NIKK), where the small molecule is obtainable by screening products of combinatorial chemistry in a luciferase system;
 - (4) treating a disease involving the activity of NIK (nuclear factor kB inducing kinase) in the pathogenesis of the disease comprising administering the cgammac or its mutein, variant, fusion protein, functional derivative, circularly permuted derivative or fragment, DNA, small molecule or antibody;
 - (5) a pharmaceutical composition comprising the cgammac or its mutein, variant, fusion protein, functional derivative, circularly permuted derivative or fragment, DNA, small molecule and antibody;
 - (6) a polypeptide fragment of cgammac, comprising the NIK binding domain, or its mutein, variant, fusion protein, functional derivative, circularly permuted derivative or its fragment;
 - (7) a DNA encoding the polypeptide fragment of NIK;
 - (8) a vector comprising the DNA;
 - (9) a cell comprising the vector;
 - (10) producing cgammac polypeptide by culturing the cell, and collecting the polypeptide produced; and
 - (11) an antibody, polyclonal or monoclonal, its chimeric antibody, fully humanized antibody, anti-anti-Id antibody, intrabody or its fragment that specifically recognizes and binds the polypeptide fragment of NIK.
- ACTIVITY - Antiinflammatory; Gastrointestinal-Gen.; Antiarthritic; Antirheumatic; Osteopathic; Antiasthmatic; Cardiant; Nootropic; Neuroprotective; Antiarteriosclerotic; Immunosuppressive; Antithyroid. No biological data given.

MECHANISM OF ACTION - Gene Therapy. No biological data given.

USE - The cgammac or its mutein, variant, fusion protein, functional derivative, circularly permuted derivative or fragment, DNA, small molecule and antibody are useful for modulating the interaction between IL-2 common gamma chain (cgammac) and NIK; and for the manufacture of a medicament for the treatment of a disease, e.g. a disease resulting from excessive immune response such as rheumatoid arthritis, osteoarthritis, inflammatory bowel disease, asthma, cardiac infarct, Alzheimer's disease or atherosclerosis; or an autoimmune

disease such as immune thyroiditis, or other arthropaties, e.g. autoimmune hemolytic anemia. The small molecule is useful for modulating signaling through cgamma (all claimed).

L6 ANSWER 4 OF 6 Elsevier Biobase COPYRIGHT 2010 Elsevier Science B.V. on
STN
DUPLICATE 1
AN 2001066571 ESBIOBASE
TI Lack of dominant-negative effects of a truncated γ c on
retroviral-mediated gene correction of immunodeficient mice
AU Candotti, Fabio; Otsu, Makoto; Sugamura, Kazuo
CS Candotti, Fabio (Clinical Gene Therapy Branch, National Human Genome
Research Institute, National Institutes of Health, 10 Center Dr,
Bethesda, MD 20892-1851 (US)); Otsu, Makoto; Sugamura, Kazuo
EMAIL: fabio@nhgri.nih.gov
SO Blood (15 Mar 2001) Volume 97, Number 6, pp. 1618-1624, 37 refs.
CODEN: BLOODW ISSN: 0006-4971
DOI: 10.1182/blood.V97.6.1618
CY United States of America
DT Journal; Article
LA English
SL English
ED Entered STN: 1 Feb 2009
Last updated on STN: 1 Feb 2009
AB A recent clinical trial of gene therapy for X-linked severe combined
immunodeficiency (XSCID) has shown that retroviral-mediated gene
correction of bone marrow stem cells can lead to the development of
normal immune function. These exciting results have been preceded by
successful immune reconstitution in several XSCID mouse models, all
carrying null mutations of the common gamma
chain (γ c). One question not formally addressed by these
previous studies is that of possible dominant-negative effects of the
endogenous mutant γ c protein on the activity
of the wild-type transferred gene product. The present work was
therefore undertaken to study whether corrective gene transfer was
applicable to an XSCID murine model with preserved expression of a
truncated γ c molecule ($\Delta\gamma$ c + -XSCID). Gene correction
of $\Delta\gamma$ c + -XSCID mice resulted in the reconstitution of
lymphoid development, and preferential repopulation of lymphoid organs
by gene-corrected cells demonstrated the selective advantage of
 γ c-expressing cells in vivo. Newly developed B cells showed
normalization of lipopolysaccharide-mediated proliferation and
interleukin-4 (IL-4)-induced immunoglobulin G1 isotype switching.
Spleenic T cells and thymocytes of treated animals proliferated normally
to mitogens and responded to the addition of IL-2, IL-4, and IL-7,
indicating functional reconstitution of γ c-sharing receptors.
Repopulated thymus showed a clear increase of CD4/CD8 - and CD8 +
fractions, both dramatically reduced in untreated $\Delta\gamma$ c +
-XSCID mice. These improvements were associated with the restoration of
Bcl-2 expression levels and enhanced cell survival. These data indicate
that residual expression of the endogenous truncated γ c did not
lead to dominant-negative effects in this murine model and suggest that
patient selection may not be strictly necessary for gene therapy of
XSCID. .COPYRG. 2001 by The American Society of Hematology.

L6 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2010 ACS on STN
AN 2000:184274 HCAPLUS
DN 132:333282
TI Intrinsic defects of B cell function in X-linked severe combined
immunodeficiency
AU White, Harry; Thrasher, Adrian; Veys, Paul; Kinnon, Christine; Gaspar,
Hubert B.

CS Molecular Immunology Unit, Institute of Child Health, University College
London, London, UK

SO European Journal of Immunology (2000), 30(3), 732-737
CODEN: EJIMAF; ISSN: 0014-2980

PB Wiley-VCH Verlag GmbH

DT Journal

LA English

AB The cytokine receptor common gamma chain
mutation in X-linked SCID results in a failure of T and NK cell
development and an as yet undefined defect of B cells. Using Ig
isotype-specific reverse transcription-PCR we show that although
hematopoietic stem cell transplantation restores a diverse repertoire of
class-switched B cell clones, on further anal. these are almost all of
donor origin. This suggests that host B cells, which predominate after
unconditioned transplantation, are still defective even in the presence of
normal T cells. These studies imply that effective humoral reconstitution
can only be achieved by the engraftment of normal donor B cells.

OSC.G 16 THERE ARE 16 CAPLUS RECORDS THAT CITE THIS RECORD (16 CITINGS)

RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 6 OF 6 MEDLINE on STN DUPLICATE 2

AN 1997174273 MEDLINE

DN PubMed ID: 9022007

TI X-SCID B cell responses to interleukin-4 and interleukin-13 are mediated
by a receptor complex that includes the interleukin-4 receptor alpha chain
(p140) but not the gamma c chain.

AU Matthews D J; Hibbert L; Friedrich K; Minty A; Callard R E

CS Immunobiology Unit, Institute of Child Health, London, GB.
(United Kingdom Wellcome Trust)

SO European journal of immunology, (1997 Jan) Vol. 27, No. 1, pp. 116-21.
Journal code: 1273201. ISSN: 0014-2980. L-ISSN: 0014-2980.

CY GERMANY: Germany, Federal Republic of

DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)

LA English

FS Priority Journals

EM 199703

ED Entered STN: 13 Mar 1997
Last Updated on STN: 6 Feb 1998
Entered Medline: 5 Mar 1997

AB This study investigates the effect of interleukin (IL)-4
mutant proteins and a monoclonal antibody to the IL-4 receptor
alpha chain on IL-4 and IL-13 response by B cells from X-linked severe
combined immunodeficiency (X-SCID) patients in which the common
gamma chain (gamma c chain) gene mutations have been
fully characterized and no gamma c chain expression was detected. In this
gamma c chain gene knockout model, it was confirmed that the gamma c chain
is essential for B cell responses to IL-2 but not for IL-4 or IL-13.
Dose-response curves for X-SCID and normal B cell responses to IL-4 were
indistinguishable, showing that the loss of the gamma c chain did not
diminish the sensitivity of B cells to IL-4. The mutant protein
IL-4(Y124D) and an antibody to the IL-4R alpha chain both inhibited
responses of X-SCID B cells to IL-4 and IL-13, showing that X-SCID B cell
responses to these cytokines are mediated by a receptor complex that
includes the IL-4R alpha chain but not the gamma c chain. Another mutant
protein, IL-4(R88D), which has greatly reduced affinity for IL-4R alpha,
was found to inhibit responses by normal B cells to IL-4 but not to IL-13.
IL-4(R88D), did not, however, inhibit X-SCID B cell responses to IL-4.
This result is consistent with IL-4(R88D) inhibition of responses mediated
by receptor complexes that include the gamma c chain. We propose that

X-SCID B cells responses to IL-4 are mediated by an IL-13 receptor complex comprised of the IL-4R alpha chain associated with the recently cloned IL-13R binding protein. This model has major implications for understanding normal B cell responses to IL-4.